

Solvent	Dilution (D) and Washing (W)	Yield(%)	N <sub>9</sub> - N <sub>7</sub> Isomers	Temp	NaOH
DMF	D: Toluene W: Toluene/Acetone		N <sub>9</sub> -(79%); N <sub>7</sub> -(18%)	160°C	+
DMF	D: Toluene W: Toluene/Acetone	93%	N <sub>9</sub> -(77%); N <sub>7</sub> -(19%)	150°C	+
DMF	D: Toluene W: Toluene/Acetone, crystallize	70%		160°C	+
DMF	D: Toluene W: Toluene/EtOH(cold)	67%		150°C	+
DMF	D: Toluene W: Toluene/Acetone, crystallize	56%		130°C	NaOEt
DMF	D: Toluene W: Toluene/EtOH(cold)		N <sub>9</sub> -(55%); N <sub>7</sub> -(12%) Un-reacted starting	160°C	-
DMF	D: Toluene W: Toluene/EtOH(cold)	70%	N <sub>9</sub> -(83%); N <sub>7</sub> -(6%)	150°C	-
DEF	D: Toluene W: Toluene/EtOH(cold)	89%	N <sub>9</sub> -(77%); N <sub>7</sub> -(21%)	150°C	+
DMA	D: Toluene W: Toluene/EtOH(cold)	70%	N <sub>9</sub> -(85%); N <sub>7</sub> -(6%)	150°C	+
DMA	D: Toluene W: Toluene/EtOH(cold)	84%	N <sub>9</sub> -(73%); N <sub>7</sub> -(19.5%)	150°C	-

Table 1

Figure 1

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Solvent	Dilution (D) and Washing (W)	Yield(%)	N <sub>9</sub> - N <sub>7</sub> Isomers	Temp	NaOH
DMA	D: None, evaporated to dryness and t-BME added W: t-BME		N <sub>9</sub> -(76%); N <sub>7</sub> -(20%)	150°C	+
DMA	D: None, evaporated to dryness and CH <sub>3</sub> CN added W: CH <sub>3</sub> CN		N <sub>9</sub> -(80%); N <sub>7</sub> -(16%)	150°C	+
DMA	D: None, evaporated to dryness and EtOH added W: EtOH	67%	N <sub>9</sub> -(90%); N <sub>7</sub> -(4%)	150°C	+
DMA	D: None, evaporated to dryness and IPA added W: IPA	84%	N <sub>9</sub> -(93%); N <sub>7</sub> -(2%)	150°C	+
DMA	D: None, evaporated to dryness and IPA/CH <sub>3</sub> CN (1:1) added W: IPA/CH <sub>3</sub> CN (1:1)		N <sub>9</sub> -(95.25%); N <sub>7</sub> -(2.49%)	150°C	+
DMA	D: Evaporated to half in volume and Toluene added W: Toluene/ EtOH(cold)	87%	N <sub>9</sub> -(76%); N <sub>7</sub> -(12%)	160°C	+
DMA	D: Evaporated to half in volume and Toluene added W: Toluene/ EtOH(cold)	89%	N <sub>9</sub> -(68%); N <sub>7</sub> -(15%)	140°C	+

Table 2

Figure 2

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Solvent	Dilution (D) and Washing (W)	Yield(%)	N <sub>6</sub> - N <sub>7</sub> Isomers	Temp	Cat
DMA	D: CH <sub>3</sub> CN W: CH <sub>3</sub> CN	89%	N <sub>6</sub> -(88%); N <sub>7</sub> -(11%)	150°C	+
DMA	D: EtOAc W: EtOAc	89%	N <sub>6</sub> -(90%); N <sub>7</sub> -(8%)	150°C	+
DMA	D: Toluene W: Toluene/EtOH (cold)	89%	N <sub>6</sub> -(95%); N <sub>7</sub> -(5%)	150°C	+
DMA	D: Toluene W: IPA (cold)	89%	N <sub>6</sub> -(86%); N <sub>7</sub> -(13%)	150°C	+
DMA	D: IPA W: IPA (cold)	89%		150°C	+
DMA	D: IPA W: IPA	87%		160°C	+
DMA	D: IPA W: IPA	82%		140°C	+
DMA	D: t-BME W: IPA	87%	N <sub>6</sub> -(95%); N <sub>7</sub> -(2-3%)	150°C	+
DMF	D: Toluene W: Toluene/EtOH (cold)		N <sub>6</sub> -(91%); N <sub>7</sub> -(3%)	Reflux	+

Table 3

Figure 3

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**HPLC METHOD**

Column	SYNERGI 5 $\mu$ , 150 x 4.6 mm Phenomenex (C18)							
Mobile Phase	A	20 mM $\text{KH}_2\text{PO}_4$ pH 6.2 Buffer (KOH)						
	B	Acetonitrile						
Flow Rate	1.00 mL/min							
Gradient Table	<table><tr><td>0-15 min</td><td>0-60% B</td></tr><tr><td>15-17 min</td><td>60-0% B</td></tr><tr><td>17-19 min</td><td>0% B</td></tr></table>		0-15 min	0-60% B	15-17 min	60-0% B	17-19 min	0% B
0-15 min	0-60% B							
15-17 min	60-0% B							
17-19 min	0% B							
Column Temperature	35 °C							
Sample Temperature	6 °C (Autosampler)							
Sample Concentration	0.5 mg /mL (Water)							
Injection Volume	10 $\mu$ L							
Detection Wavelength	220, 270 nm							

Figure 4

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WO 2004/014912

PCT/US2002/025540

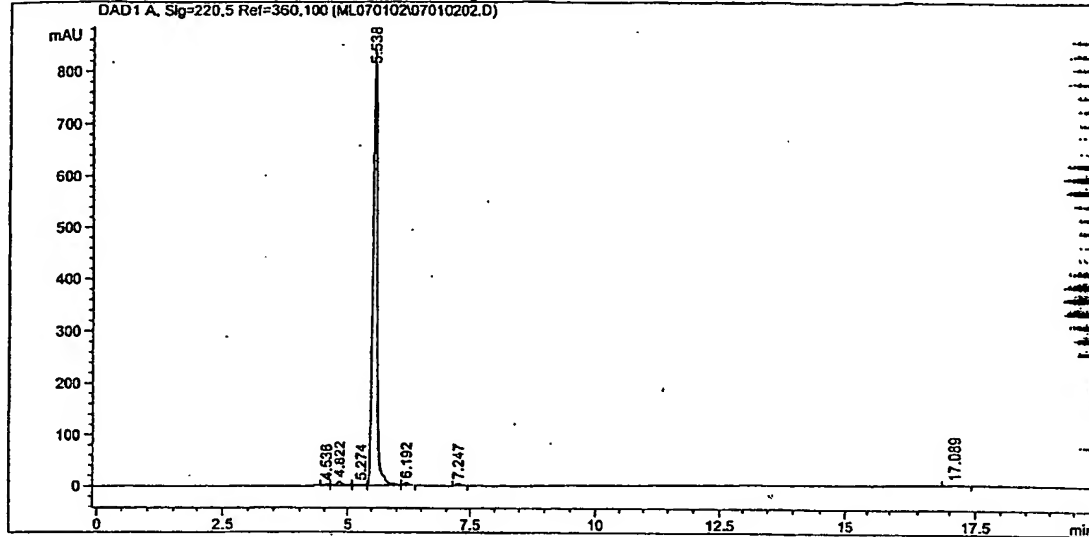
ata File C:\HPCHEM\1\DATA\ML070102\07010202.D

Sample Name: ICN373

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=====
Injection Date : 7/1/2002 5:16:33 PM      Seq. Line : 2
Sample Name    : ICN373-87                Location  : Vial 1
Acq. Operator  : Mike Landesman           Inj       : 1
                                           Inj Volume: 5 µl
Acq. Method    : C:\HPCHEM\1\METHODS\ICN34952.M
Last changed   : 6/14/2002 11:49:33 AM by Mike Landesman
Analysis Method: C:\HPCHEM\1\METHODS\ICN34929.M
Last changed   : 6/25/2002 8:19:23 AM by Mike Landesman
=====
DAD1 A, Sig=220,5 Ref=360,100 (ML070102\07010202.D)

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Area Percent Report
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Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000

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Signal 1: DAD1 A, Sig=220,5 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.536	VV	0.1116	22.60877	3.00970	0.4351
2	4.822	VV	0.1320	74.46996	8.04190	1.4331
3	5.274	VV	0.1676	18.32598	1.48883	0.3527
4	5.538	VV	0.0929	5003.10547	847.37561	96.2821
5	6.192	VB	0.1016	35.53940	5.34228	0.6839
6	7.247	PB	0.0963	24.99750	4.03450	0.4811
7	17.089	BB	0.2136	17.25084	1.21556	0.3320

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Totals :                5196.29793  870.50839
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Figure 5

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